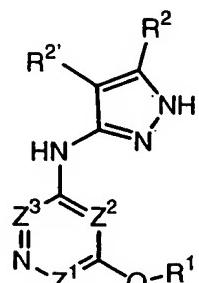


We claim:

1. A compound of formula III:



III

or a pharmaceutically acceptable derivative or prodrug thereof, wherein:

Z^1 is nitrogen or CR^8 , Z^2 is nitrogen or CH , and Z^3 is nitrogen or CR^x , provided that one of Z^1 and Z^3 is nitrogen;

R^x is $T-R^3$ or $L-Z-R^3$;

Q is selected from $-N(R^4)-$, $-O-$, $-S-$, or $-CH(R^6)-$;

R^1 is $T-(\text{Ring D})$;

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein each substitutable ring carbon of Ring D is independently substituted by oxo, $T-R^5$, or $V-Z-R^5$, and each substitutable ring nitrogen of Ring D is independently substituted by $-R^4$;

T is a valence bond or a C_{1-4} alkylidene chain, wherein when Q is $-CH(R^6)-$, a methylene unit of said C_{1-4}

alkylidene chain is optionally replaced by -O-, -S-, -N(R⁴)-, -CO-, --OC(O)NH-, or -NHCO₂-;

Z is a C₁₋₄ alkylidene chain;

L is -O-, -S-, -SO-, -SO₂-, -N(R⁶)SO₂-, -SO₂N(R⁶)-, -N(R⁶)-, -CO-, -CO₂-, -N(R⁶)CO-, -N(R⁶)C(O)O-, -N(R⁶)CON(R⁶)-, -N(R⁶)SO₂N(R⁶)-, -N(R⁶)N(R⁶)-, -C(O)N(R⁶)-, -OC(O)N(R⁶)-, -C(R⁶)₂O-, -C(R⁶)₂S-, -C(R⁶)₂SO-, -C(R⁶)₂SO₂-, -C(R⁶)₂SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)-, -C(R⁶)₂N(R⁶)C(O)-, -C(R⁶)₂N(R⁶)C(O)O-, -C(R⁶)=NN(R⁶)-, -C(R⁶)=N-O-, -C(R⁶)₂N(R⁶)N(R⁶)-, -C(R⁶)₂N(R⁶)SO₂N(R⁶)-, or -C(R⁶)₂N(R⁶)CON(R⁶)-;

R² and R^{2'} are independently selected from -R, -T-W-R⁶, or R² and R^{2'} are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable ring carbon of said fused ring formed by R² and R^{2'} is independently substituted by halo, oxo, -CN, -NO₂, -R⁷, or -V-R⁶, and each substitutable ring nitrogen of said ring formed by R² and R^{2'} is independently substituted by R⁴;

R³ is selected from -R, -halo, -OR, -C(=O)R, -CO₂R, -COCOR, -COCH₂COR, -NO₂; -CN, -S(O)R, -S(O)₂R, -SR, -N(R⁴)₂, -CON(R⁷)₂, -SO₂N(R⁷)₂, -OC(=O)R, -N(R⁷)COR, -N(R⁷)CO₂(C₁₋₆ aliphatic), -N(R⁴)N(R⁴)₂, -C=NN(R⁴)₂, -C=N-OR, -N(R⁷)CON(R⁷)₂, -N(R⁷)SO₂N(R⁷)₂, -N(R⁴)SO₂R, or -OC(=O)N(R⁷)₂;

each R is independently selected from hydrogen or an optionally substituted group selected from C₁₋₆ aliphatic, C₆₋₁₀ aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R⁴ is independently selected from -R⁷, -COR⁷,
-CO₂(optionally substituted C₁₋₆ aliphatic), -CON(R⁷)₂,
or -SO₂R⁷;

each R⁵ is independently selected from -R, halo, -OR,
-C(=O)R, -CO₂R, -COCOR, -NO₂, -CN, -S(O)R, -SO₂R, -SR,
-N(R⁴)₂, -CON(R⁴)₂, -SO₂N(R⁴)₂, -OC(=O)R, -N(R⁴)COR,
-N(R⁴)CO₂(optionally substituted C₁₋₆ aliphatic),
-N(R⁴)N(R⁴)₂, -C=NN(R⁴)₂, -C=N-OR, -N(R⁴)CON(R⁴)₂,
-N(R⁴)SO₂N(R⁴)₂, -N(R⁴)SO₂R, or -OC(=O)N(R⁴)₂;

V is -O-, -S-, -SO-, -SO₂-, -N(R⁶)SO₂-, -SO₂N(R⁶)-,
-N(R⁶)-, -CO-, -CO₂-, -N(R⁶)CO-, -N(R⁶)C(O)O-,
-N(R⁶)CON(R⁶)-, -N(R⁶)SO₂N(R⁶)-, -N(R⁶)N(R⁶)-,
-C(O)N(R⁶)-, -OC(O)N(R⁶)-, -C(R⁶)₂O-, -C(R⁶)₂S-,
-C(R⁶)₂SO-, -C(R⁶)₂SO₂-, -C(R⁶)₂SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)-,
-C(R⁶)₂N(R⁶)C(O)-, -C(R⁶)₂N(R⁶)C(O)O-, -C(R⁶)=NN(R⁶)-,
-C(R⁶)=N-O-, -C(R⁶)₂N(R⁶)N(R⁶)-, -C(R⁶)₂N(R⁶)SO₂N(R⁶)-, or
-C(R⁶)₂N(R⁶)CON(R⁶)-;

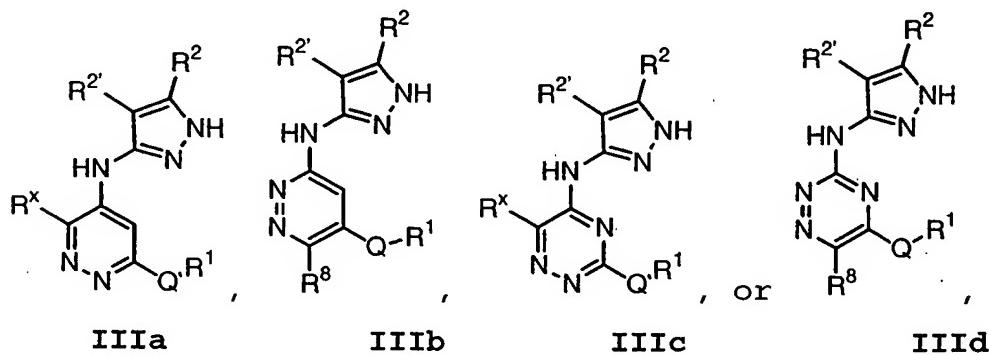
W is -C(R⁶)₂O-, -C(R⁶)₂S-, -C(R⁶)₂SO-, -C(R⁶)₂SO₂-,
-C(R⁶)₂SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)-, -CO-, -CO₂-,
-C(R⁶)OC(O)-, -C(R⁶)OC(O)N(R⁶)-, -C(R⁶)₂N(R⁶)CO-,
-C(R⁶)₂N(R⁶)C(O)O-, -C(R⁶)=NN(R⁶)-, -C(R⁶)=N-O-,
-C(R⁶)₂N(R⁶)N(R⁶)-, -C(R⁶)₂N(R⁶)SO₂N(R⁶)-,
-C(R⁶)₂N(R⁶)CON(R⁶)-, or -CON(R⁶)-;

each R⁶ is independently selected from hydrogen or an
optionally substituted C₁₋₄ aliphatic group, or two R⁶
groups on the same nitrogen atom are taken together
with the nitrogen atom to form a 5-6 membered
heterocyclyl or heteroaryl ring;

each R⁷ is independently selected from hydrogen or an
optionally substituted C₁₋₆ aliphatic group, or two R⁷
on the same nitrogen are taken together with the
nitrogen to form a 5-8 membered heterocyclyl or
heteroaryl ring; and

R^8 is selected from -R, halo, -OR, -C(=O)R, -CO₂R, -COCOR, -NO₂, -CN, -S(O)R, -SO₂R, -SR, -N(R⁴)₂, -CON(R⁴)₂, -SO₂N(R⁴)₂, -OC(=O)R, -N(R⁴)COR, -N(R⁴)CO₂(optionally substituted C₁₋₆ aliphatic), -N(R⁴)N(R⁴)₂, -C=NN(R⁴)₂, -C=N-OR, -N(R⁴)CON(R⁴)₂, -N(R⁴)SO₂N(R⁴)₂, -N(R⁴)SO₂R, or -OC(=O)N(R⁴)₂.

2. The compound according to claim 1, wherein Q is -N(R⁴)-, -S-, or -CH(R⁶)-, and said compound is of formula IIIa, IIIb, IIIc, or IIId:



or a pharmaceutically acceptable derivative or prodrug thereof.

3. The compound according to claim 2, wherein said compound has one or more features selected from the group consisting of:

- (a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C₁₋₄ aliphatic group;
- (b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;
- (c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is $-R$ or $-T-W-R^6$ and R^2' is hydrogen, or R^2 and R^2' are taken together to form an optionally substituted benzo ring.

4. The compound according to claim 3, wherein:

(a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;

(b) R^1 is $T-(\text{Ring D})$, wherein T is a valence bond or a methylene unit;

(c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is $-R$ or $-T-W-R^6$ and R^2' is hydrogen, or R^2 and R^2' are taken together to form an optionally substituted benzo ring.

5. The compound according to claim 3, wherein said compound has one or more features selected from the group consisting of:

(a) R^1 is $T-(\text{Ring D})$, wherein T is a valence bond, and Q is $-S-$ or $-NH-$;

(b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(c) R^2 is $-R$ and R^2' is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

6. The compound according to claim 5, wherein:

(a) R^1 is $T-(\text{Ring D})$, wherein T is a valence bond, and Q is $-S-$ or $-NH-$;

(b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(c) R^2 is $-R$ and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C₁₋₆ aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

7. The compound according to claim 5, wherein said compound has one or more features selected from the group consisting of:

- (a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;
- (b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO₂, -N(R⁴)₂, optionally substituted C₁₋₆ aliphatic group, -OR, -CO₂R, -CON(R⁴)₂, -OCO(R⁴)₂, -N(R⁴)COR, -N(R⁴)SO₂R, -N(R⁶)COCH₂CH₂N(R⁴)₂, or -N(R⁶)COCH₂CH₂CH₂N(R⁴)₂; and
- (c) R^2 is hydrogen or a substituted or unsubstituted C₁₋₆ aliphatic.

8. The compound according to claim 7, wherein:

- (a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;
- (b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO₂, -N(R⁴)₂, optionally substituted C₁₋₆ aliphatic group, -OR, -CO₂R, -CON(R⁴)₂, -OCO(R⁴)₂,

$-N(R^4)COR$, $-N(R^4)SO_2R$, $-N(R^6)COCH_2CH_2N(R^4)_2$, or
 $-N(R^6)COCH_2CH_2CH_2N(R^4)_2$; and

(c) R^2 is hydrogen or a substituted or unsubstituted
 C_{1-6} aliphatic.

9. A compound selected from the group consisting
of:

$N^5-(1H-Indazol-6-yl)-N^3-(5-methyl-1H-pyrazol-3-yl)-[1,2,4]triazine-3,5-diamine$;

$N-\{4-[3-(5-Methyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-5-ylsulfanyl]-phenyl\}-acetamide$;

$[5-(3-Methoxy-benzyl)-[1,2,4]triazin-3-yl]-(5-methyl-1H-pyrazol-3-yl)-amine$;

$N^3-(5-Cyclopropyl-1H-pyrazol-3-yl)-N^5-pyridin-3-ylmethyl-[1,2,4]triazine-3,5-diamine$;

$[5-(Benzothiazol-6-ylsulfanyl)-[1,2,4]triazin-3-yl]-(5-cyclopropyl-1H-pyrazol-3-yl)-amine$;

$\{4-[3-(5-Cyclopropyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-5-yloxy]-phenyl\}-acetonitrile$;

$N-\{4-[3-(1H-Indazol-3-ylamino)-[1,2,4]triazin-5-ylamino]-phenyl\}-methanesulfonamide$;

$(1H-Indazol-3-yl)-[5-(thiophen-2-ylmethylsulfanyl)-[1,2,4]triazin-3-yl]-amine$;

$N^5-(5-Methyl-1H-pyrazol-3-yl)-N^3-pyridin-3-ylmethyl-[1,2,4]triazine-3,5-diamine$;

$[3-(Benzothiazol-6-ylsulfanyl)-[1,2,4]triazin-5-yl]-(5-methyl-1H-pyrazol-3-yl)-amine$;

$\{4-[5-(5-Methyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-3-yloxy]-phenyl\}-acetonitrile$;

$N^5-(5-Cyclopropyl-1H-pyrazol-3-yl)-N^3-(1H-indazol-6-yl)-[1,2,4]triazine-3,5-diamine$;

$N-\{4-[5-(5-Cyclopropyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-3-ylsulfanyl]-phenyl\}-acetamide$;

N⁵-(1*H*-Indazol-3-yl)-N³-(1*H*-indazol-6-yl)-
[1,2,4]triazine-3,5-diamine;
(1*H*-Indazol-3-yl)-[3-(3-methoxy-phenylsulfanyl)-
[1,2,4]triazin-5-yl]-amine;
N⁵-(1*H*-Indazol-6-yl)-N³-(5-methyl-1*H*-pyrazol-3-yl)-
pyridazine-3,5-diamine;
N-{4-[6-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-
ylsulfanyl]-phenyl}-acetamide;
[5-(3-Methoxy-benzyl)-pyridazin-3-yl]- (5-methyl-1*H*-
pyrazol-3-yl)-amine;
N³-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N⁵-pyridin-3-
ylmethyl-pyridazine-3,5-diamine;
[5-(Benzothiazol-6-ylsulfanyl)-pyridazin-3-yl]- (5-
cyclopropyl-1*H*-pyrazol-3-yl)-amine;
{4-[6-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-
yloxy]-phenyl}-acetonitrile;
N-{4-[6-(1*H*-Indazol-3-ylamino)-pyridazin-4-ylamino]-
phenyl}-methanesulfonamide;
(1*H*-Indazol-3-yl)-[5-(thiophen-2-ylmethylsulfanyl)-
pyridazin-3-yl]-amine;
N⁵-(5-Methyl-1*H*-pyrazol-3-yl)-N³-pyridin-3-ylmethyl-
pyridazine-3,5-diamine;
[6-(Benzothiazol-6-ylsulfanyl)-pyridazin-4-yl]- (5-
methyl-1*H*-pyrazol-3-yl)-amine;
{4-[5-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-
yloxy]-phenyl}-acetonitrile;
N⁵-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N³-(1*H*-indazol-6-
yl)-pyridazine-3,5-diamine;
N-{4-[5-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-
3-ylsulfanyl]-phenyl}-acetamide;
N⁵-(1*H*-Indazol-3-yl)-N³-(1*H*-indazol-6-yl)-pyridazine-
3,5-diamine; and

(1*H*-Indazol-3-yl)-[6-(3-methoxy-phenylsulfanyl)-pyridazin-4-yl]-amine.

10. A composition comprising a compound according to any of claims 1-9, and a pharmaceutically acceptable carrier.

11. The composition according to claim 10, further comprising an additional therapeutic agent.

12. A method of inhibiting Aurora-2 or GSK-3 activity in a biological sample comprising the step of contacting said biological sample with a compound according to any one of claims 1-9.

13. A method of inhibiting Aurora-2 activity in a patient comprising the step of administering to said patient a composition according to claim 10.

14. A method of inhibiting Aurora-2 activity in a patient comprising the step of administering to said patient a composition according to claim 11.

15. A method of treating an Aurora-2-mediated disease, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

16. The method according to claim 15, wherein said disease is selected from colon, breast, stomach, or ovarian cancer.

17. The method according to claim 16, wherein said method further comprises administering an additional therapeutic agent.

18. The method according to claim 17, wherein said additional therapeutic agent is a chemotherapeutic agent.

19. A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 10.

20. A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 11.

21. A method of method of treating a GSK-3-mediated disease, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

22. The method according to claim 21, wherein said GSK-3-mediated disease is selected from diabetes, Alzheimer's disease, Huntington's Disease, Parkinson's Disease, AIDS-associated dementia, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusion/ischemia, or baldness.

23. The method according to claim 22, wherein said GSK-3-mediated disease is diabetes.

24. A method of enhancing glycogen synthesis or lowering blood levels of glucose in a patient in need

thereof, which method comprises administering to said patient a therapeutically effective amount of a composition according to claim 10.

25. A method of inhibiting the production of hyperphosphorylated Tau protein in a patient, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.

26. A method of inhibiting the phosphorylation of β -catenin, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.